THE EFFECT OF HDAC INHIBITORS ON RETINAL DEVELOPMENT OF CHICK EMBRYO

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Introduction: Gene expression is regulated by the accessibility of regulatory cis-acting DNA elements as well as availability of transcription factors. Histone deacetylase (HDAC) can regulate gene expression by deacetylating histone tails, which leads to a closed conformation of the DNA/histone complex and generally a reduction in expression. HDACs have been proposed to play a key role in cell survival, proliferation and differentiation; however, fewer studies have been focusing on the role of HDACs in the developing vertebrate retina.
Methods: Chick retinal explants were treated with vehicle (dimethyl sulphoxide(DMSO)) or 1.0 μM Trichstatin A (TSA), a known inhibitor of class 1 and 2 HDACs. Immunohistochemistry (IHC) was performed to analyze the levels of cleaved caspase 3, a protein activated during apoptosis, phospho-histone 3 (pH3) marker for mitotic phase, SOX2 which marks progenitor cells, and Islet-1 which marks differentiated cells. Digital images were analyzed using Image J/FIJI software for numbers of labeled cells.
Results: After treatment with control or TSA, numbers of progenitor and differentiating cells were quantified. TSA-treated samples showed a statistically significant increase in SOX2+ (progenitors) and an increase in islet-1+ (differentiating) cells. To assess if any differences in proliferation and/or cell death that might lead to an increase in the number of progenitor and differentiating cells, samples were labeled for pH3 or cleaved caspase 3. Treatment with TSA led to increases in cells positive for pH3 and a statistically significant increase in cells positive for cleaved caspase 3 compared to controls.
Conclusions: HDAC inhibitor, TSA, increased the number of progenitor and differentiating cells by increasing proliferation within the developing retina. However, there was also an increase in the number of cells undergoing apoptosis. Ongoing studies will determine which HDACs may be responsible for these results.

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